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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,727	01/17/2002	Graham D. Cook	AM100535	2584

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

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01/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/046,727	COOK ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/2/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-13 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-13,26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed October 2, 2007 have been received and entered into the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-13 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to claims 1 and 26-30, the newly added limitation "tablet or caplet is **not enterically** coated" was not literally or implicitly described with reasonable clarity in the claims or any other portion of the originally filed specification. The description does not convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention.

With regard to claims 6-13, and 27, the newly added limitation of "**food** coloring", being "**optionally**" employed in the instant composition. The employment of "**sorbitol,**

and sorbitans" utilized as two separate generic compounds rather than "an aqueous solution of specific form, D-sorbitol and sorbitans" (see specification page 15) were not literally or implicitly described with reasonable clarity in the claims or any other portion of the originally filed specification. The description does not convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention. Applicants assert that support for the amendment can be found in the specification on page 15, lines 11-20, and Table 1 on page 20. However, **no such support** for employment of genus of "food" coloring, sorbitol and sorbitans as a two separate compounds, and the food coloring and potassium hydroxide as being employed as **an option**.

This is a New Matter rejection.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gullapalli (U.S.Patent No. 6,251,426 B1) in view of Denton et al. (U.S.Patent No. 5,104,648) and Takase et al. (U.S.Patent No. 6,248,347 B1).

Gullapalli teaches composition consisting essentially of ibuprofen, PEG 600, Kollidon 17 PF (polyvinylpyrrolidone having approximate molecular weight of 10,000) can be encapsules with sheath ingredients consisting essentially of gelatin, sorbitol special (a mixture of sorbitol and sorbitan), maltitol and water. (Example 8, Example 11, column 3, lines 5-15, column 4, lines 3-5 and lines 37-45). Gullapalli teaches the composition can have other ingredients such as diphenhydramine hydrochloride (an antihistamine). (column 2, lines 43-48, claims 5 and 17). Gullapalli teaches the effective dosage of ibuprofen be at least 175mg, and preferably about 200mg. (column 4, lines 28-30). These dosages are within Applicant's dosage set forth in claim 7 and preferred dosage of 200mg is the same as recited amount in instant claim 8. Gullapalli teaches the softgel capsule should be of a size that is easily swallowed and generally, the fill size of the capsule will be less than 600mg, and preferably about 500mg, or less in order for the capsule to be an acceptably small dimension. (column 4, lines 23-29). Gullapalli teaches the percentages of the formulation may also have up to 10% of an antihistamine, such as diphenhydramine hydrochloride. (column 2, lines 42-48). Gullapalli teaches the amount of diphenhydramine hydrochloride expressed in percentages but does not teach the specific amounts in mg set forth in claims 10-13 and the specified citrate salt set forth in claims 12 and 13.

Gullapalli does not exclude Kollidon 17 PF and Maltitol in the above composition.

Denton et al. teach that in ibuprofen-PVP (polyvinylpyrrolidone) formulation, the higher molecular weight products of PVP, 600,000 Daltons and above cause eutectic formulation during storage at elevated temperatures. (column 2, lines 45-50).

Takase et al. teach that maltitol ingestion causes symptoms such as diarrhea. (column 1, lines 50-55).

It would have been obvious to one of ordinary skill in the art to modify the ibuprofen composition of Gullapalli and exclude Kollidon 17 PF (polyvinylpyrrolidone (PVP) having approximate molecular weight of 10,000) and maltitol in his illustrated examples 8 and 11 because PVP such as Kollidon 17 PF utilized by Gullapalli cause problem with ibuprofen in a single formulation in view of Denton et al. and because maltitol can cause diarrhea in view of Takase et al. One would have been motivated to eliminate those two agents from Gullapalli's composition in order to achieve a stable composition with a long shelf-life devoid of eutectic mixture and undesired effect, e.g. diarrhea.

It would have been obvious to one of ordinary skill in the art to employ an amount of diphenhydramine up to 10% of preferred 500mg soft gel capsules taught by Gullapalli as preferred amount of diphenhydramine content because Gullapalli teaches that up to 10% diphenhydramine up to 50mg (10% of 500mg softgel) is useful as suggested by Gullapalli as an additional ingredient. One of ordinary skill in the art would have been motivated to employ diphenhydramine in any workable range up to 50mg in Gullapalli's softgel composition in order to provide antihistamine effect addition to non-steroidal anti-inflammatory effect of ibuprofen for convenient single formulation comprising dual

therapeutic effect. There is a reasonable expectation of successfully formulating 500mg softgel capsules that are easily swallowed by employing **up to 10% (up to 50mg)** of diphenhydramine because all the ingredients including active agents, binders in the formulations are all well taught and suggested by Gullapalli.

Claims 1 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) in view of Weng et al. (U.S.Patent No. 5,512,300).

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in **tablet form or two (bilayer) or more layered tablets.** (column 8, lines 4-10). Sunshine et al. teach that the tablet form or capsule comprising ibuprofen and diphenhydramine can be **impregnated with polymeric matrices**. (column 8, lines 1-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65).

Sunshine et al. do not teach the separation of ibuprofen and diphenhydramine in different layers.

Weng et al. report that it has been recognized that solid dosage forms such as tablets containing ibuprofen and other ingredients tend to exhibit stability problems, including the formulation of low melting point eutectics. (column 1, lines 13-20). Weng et al. report ibuprofen forms low melting point eutectics with diphenhydramine hydrochloride. (column 1, lines 55-57).

It would have been obvious to one of ordinary skill in the art to separate diphenhydramine and ibuprofen in different layers of Sunshine's two layered tablet (bilayer) because diphenhydramine and ibuprofen in a solid dosage forms such as tablets tend to exhibit stability problems including the formation of eutectics as taught by Weng et al. and because Sunshine teaches that the composition can be formulated in two or more layered tablets. One would have been motivated to separate ibuprofen and diphenhydramine bilayer tablet taught by Sunshine so that they are placed into physically discrete region of two different layers of bilayer tablet in order to avoid the eutectic stability problems of solid dosage form comprising diphenhydramine and ibuprofen reported by Wang et al. There is a reasonable expectation of successfully formulating Sunshine's two layered (bilayer) tablet by separating ibuprofen and diphenhydramine in order to achieve more stable bilayer tablet without the problems of forming a eutectic mixture.

Claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) in view of Weng et al. (U.S.Patent No. 5,512,300) as applied to claims 1 and 7-13 and further Drug Facts and Comparisons, 1997 Edition, all of record.

Sunshine et al's teaching as applied as before and additional teachings as follows:

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). **Sunshine et al. teach that "propionic acid derivatives" including ibuprofen is defined as non-narcotic analgesics/nonsteroidal anti-inflammatory drugs having free –CH(CH3)COOH. (column 5, lines 1-20, particularly, lines 12-15).** Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in tablet form or two or more layered tablets. (column 8, lines 4-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65). **Sunshine et al. teach that the composition can be formulated with for oral administration in the form of tablets or capsules with any oral non-toxic pharmaceutically acceptable inert carrier such as lactose, starch cellulose and carboxymethylcellulose. (column 7, lines 15-45).**

Weng et al's teachings as applied as before.

Sunshine et al. and Weng et al. do not teach the onset of action of the composition of within 60 minutes.

Drug Facts and Comparisons teach that onset of action of antihistamines including diphenhydramine is within 15 to 30 minutes (page 1135, under

Antihistamines: Dosage and Effects; page 1136 under Pharmacokinetics). Drug Facts and Comparisons teach that onset of action of ibuprofen is 0.5 hour (30 minutes). (Page 1387, under pharmacokinetic parameters).

It would have been obvious to one of ordinary skill in the art that the bilayer tablet comprising ibuprofen and diphenhydramine taught by Sunshine et al. as modified by Weng et al. would have an effect within 60 minutes as claimed by the Applicants because Drug Facts and Comparison teaches that each of the active agents have onset of action within 30 minutes. It is expected that the combination of two agents would possess same onset of action as well-known by the cited reference.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Response to Arguments

Applicants' arguments filed October 2, 2007 have been fully considered but they are not persuasive. Applicants argue that the disclosure of the specification demonstrates that Applicants were in possession of the claimed composition in tablets or caplet not enterically coated because Example 2 provides a detailed description of the manufacture of bilayer caplets falling within the scope of the invention describing

coating of the formulation using Opadry II blue, followed by dusting with calcium stearate. Applicants further argue that the specification on page 23, line 9 to page 24, line 2, shows no other coating is added and that the enclosed print-out from the manufacturer of Opadry II Blue (Colorcon), the manufacturer markets several coating formulations, including "Sureteric", or enteric or delayed release formulations. This is not persuasive because possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings for in structural chemical formulas which permit a person skilled in the art to clearly recognized that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognized that the inventor had possession of the claimed invention. However, in this case, Applicants have not conveyed possession of the invention with reasonable clarity to one skilled in the art. Claim recites the limitation "not **enterically** coated". Claim is read in light of the specification and although the terms of a claim drawn to "coated" has literal support, the specific "coating" being "enteric" lack literal support and inconsistent with the specification disclosure because the tablets and capsules not specifically being **enterically** coated is not described in the original disclosure. Therefore, the description does not convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the specific "**enteric**" coating. Therefore, the new matter rejection made in this Office Action is deemed proper. Applicants argue

that Gullapalli teaches capsules comprising polyetheylene glycol (PEG) and polyvinylpyrrolidone (PVP) and that Gullapalli provides no reason why the skilled artisan would arrive at a composition consisting essentially of, gelatin, water, sorbitol, sorbitans, ibuprofen and diphenhydramine in amounts effective to treat a pain associated sleep disturbance and optionally food coloring and potassium hydroxide formulated in a soft gelatin capsule. This is not found persuasive because Denton et al. teach that particular PVP employed by Gullapalli combined with ibuprofen cause problems in storage due to formation of eutectic mixture. Therefore, one of ordinary skill in the art would be motivated to exclude the PVP utilized by Gullapalli in order to avoid the storage problem taught by Denton et al.

Applicants argue that Sunshine et al. do not teach the separation of ibuprofen and diphenhydramine in different layers and Weng does not provide a reason for separating the actives into two layers. This is not found persuasive because Weng et al. report the recognized stability problems between ibuprofen and diphenhydramine in a solid dosage forms while Sunshine et al. teach that the ibuprofen and diphenhydramine can be formulated in tablet having two (bilayer) or more layered tablets. One would have been motivated to separate ibuprofen and diphenhydramine bilayer tablet taught by Sunshine so that they are placed into physically discrete region of two different layers of bilayer tablet in order to avoid the eutectic stability problems of solid dosage form comprising diphenhydramine and ibuprofen reported by Weng et al. Applicants argue that claims 27-30 have been amended to recite a formulation in which the ibuprofen is not enterically coated. This is not found persuasive because recite a

formulation which the ibuprofen is not **enterically** coated deemed to fail to patentably distinguish over the state of the art as represented by the cited references because Sunshine et al. teaches the compression comprising ibuprofen and diphenhydramine can be formulated as sustained release including layered tablets containing layers of varying disintegration rates or controlled release polymeric matrices impregnated with the active composition and do not mention any "enteric coating". Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

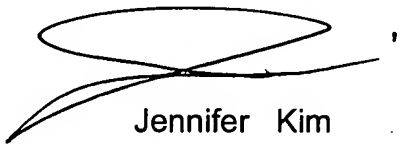
Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Jennifer Kim

Primary Examiner
Art Unit 1617

Jmk
December 27, 2007